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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/902,432	07/10/2001	Irwin Gelman	A30558-A-FWC-A	8487

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EXAMINER	
PRIEBE, SCOTT DAVID	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 08/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/902,432	GELMAN, IRWIN	
	Examiner	Art Unit	
	Scott D. Priebe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 April 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

The benefit claim filed on 6/14/04 was not entered because the required reference was not timely filed within the time period set forth in 37 CFR 1.78(a)(2) or (a)(5). If the application is an application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a nonprovisional application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the reference to the prior application must be made during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). If applicant desires priority under 35 U.S.C. 120 based upon a previously filed application, applicant must file a petition for an unintentionally delayed benefit claim under 37 CFR 1.78(a)(3) or (a)(6). The petition must be accompanied by: (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted); (2) a surcharge under 37 CFR

1.17(t); and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications.

Applicant had provided a preliminary amendment (Transmittal paper, addendum page 2, filed 7/10/01) to the specification that provided the required "specific reference" for applications 08/978,277 and 08/665,401, but not for application 08/635,121. Although a reference to the '121 application appears in the text of the amendment, it is not a "specific reference" as required by 37 CFR 1.78(a)(2) and (a)(5) because it does not include the relationship (i.e. continuation, divisional, or continuation-in-part) for the '121 application. This deficiency in the reference to the '121 application was reflected in the filing receipt mailed to applicant, which did not list the '121 application under "Continuing Data".

As indicated in the previous Office action, none of the '277, '401, or '121 applications provide support as per 35 USC 112, 1st para. for the claimed invention, as required under 35 USC 120.

Specification

The specification remains objected to as failing to provide proper antecedent basis for the claimed subject matter for the reasons of record set forth in the Office action of 12/18/02. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o).

Applicant's arguments filed 6/14/04 have been fully considered but they are not persuasive. Page 33, lines 3-11, of the specification does not provide antecedent basis for the claim terminology. It does not mention any SSeCKS variant having increased affinity for cyclin D. Inserting the test of original claim 15 at this location would provide antecedent basis for the claim terminology.

Claim Rejections - 35 USC § 112

Claim 15 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a rejection for introduction of new matter into the claim.

Claim 15 has been amended to recite that the increased affinity for cyclin D was in comparison to wild type SSeCKs polypeptide. Applicant has not indicated where or how the original specification supports this new limitation, as is Applicant's burden, MPEP 714.02, last sentence of the third paragraph from the end and 2163.06 (I) last sentence. There is no support for this new limitation. The sole description for the embodiment of the invention of original

claim 15 was the claim itself. Original claim 15 did not indicate a reference for determining "increased affinity," much less indicate that wild-type SSeCKs polypeptide was that reference.

Claims 14 and 15 remain rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in the Office action of 12/18/02 as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 14 was inadvertently omitted from the first sentence of the rejection as set forth in the previous Office action, although specific grounds of rejection of claim 14 were set forth. Applicant's response has addressed the grounds of rejection of claim 14, and so it is implicit that Applicant understood that claim 14 had been rejected for lack of adequate written description. Claim 13 was not and is not rejected on these grounds.

Applicant's arguments filed 6/14/04 have been fully considered but they are not persuasive. With respect to claim 14, Applicant indicates that cytoskeletal anchoring peptides were known in the art and it was therefore unnecessary to disclose such, and refers to two publications cited in the specification at page 40, lines 10-11. However, neither of these references have been made of record to determine whether cytoskeletal anchoring peptides were in fact known in the art. The incorporation of these non-patent publications by reference (as indicated on page 120) is improper because the publications are not US patents and because the specification does not clearly indicate for what the publication are being relied upon, or where in the publications the incorporated teachings are to be found. See *Advanced Display Systems Inc.*

v. Kent State University, 54 USPQ2d 1673 (CAFC 2000) at 1676. One of these, Diviani et al. (J. Cell. Sci. 114 (8): 1431-1437, 2001) is a review of AKAP proteins, which includes SSeCKs (a.k.a. gravin, see page 1434). While Diviani dislcoses that some AKAP proteins bind cytoskeletal proteins, e.g SSeCKs which binds actin, it does not disclose any nucleic acid or amino acid sequence information for these proteins, and more important, does not identify the peptide region of any AKAP proteins that binds to cytoskeletal components, i.e. the cytoskeletal anchoring peptides.

With respect to claim 15, Applicant argues that the specification provides the SSeCKs nucleotide sequence, identifies the CY domain as the cyclin D binding domain and provides an assay for cyclin D binding, and asserts that given this information one of skill in the art could identify SSeCKs polypeptides with increased binding affinity for cyclin D. However, this rejection is not directed to a lack of enablement for making such variants, but for lack of adequate written description of such variants and lack of evidence that Applicant was in possession of such variants. At best the specification provides a potential method for making SSeCKs polypeptides with increased binding affinity for cyclin D. However, the courts and the Board have repeatedly held (*Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*,18 USPQ2d 1016 (CA FC, 1991); *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993); *Fiddes v. Baird*, 30 USPQ2d 1481 (BPAI 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)) that an adequate written description of a nucleic acid requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, irrespective of the complexity or simplicity of the method; what is required is a description of the nucleic acid

itself. That Applicant suggests one of skill in the art could go make the recited variants for themselves is tacit admission that Applicant was not in possession of such variants.

Claim 13 remains rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in the Office action of 12/18/02, because the specification, while being enabling for a method for inhibiting cell proliferation in cultured cells, does not reasonably provide enablement for inhibiting cell proliferation *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 14 and 15 remain rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in the Office action of 12/18/02 as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's arguments filed 6/14/04 have been fully considered but they are not persuasive. Applicant cites Xia et al. (Cancer Res. 61: 5644-5651, Jul. 2001), provided as an exhibit, as evidence that the claimed invention is enabled for treating cancer. However, this evidence is not commensurate in scope with the claims, which embrace any use for the claimed method for inhibiting cell proliferation *in vivo*. Furthermore, the evidence provided in Xia is not analogous to the treatment of cancer, which would require transfection of cancer cells *in situ* in a patient. The experiment disclosed in Xia involved ectopic implantation of selected human prostate tumor cells that had been previously transfected with a vector expressing SSeCKs. This model represents an idealized situation in which all tumors cells in a subject would be

transfected with a gene therapy vector. As indicated in Orkin, one of the problems in gene therapy was inadequate gene transfer. This model cannot and does not take such difficulties into account. Also, the results indicated that derepression of SSeCKs expression mildly inhibited growth of the primary tumor at 8-10 days after derepression, but the inhibition was only temporary and tumor growth comparable to the control resumed. A substantial inhibitory effect was seen on metastasis. However, the instant specification does not suggest that the instant method would have that use.

Gomez-Navarro et al. (Eur. J. Cancer 35 (6): 867-885, Jun. 1999) reviews the state of cancer gene therapy before the instant invention was made. The instant invention falls into the general strategy of mutation compensation, which includes treatment with vectors expressing tumor suppressors and promoters of apoptosis. The reference indicates that gene therapy for delivery of p53, RB1 and BRCA1 were being studied in human clinical trials. The reference discloses that even after delivery of tumor suppressor genes, some tumors show persistent tumorogenicity and proliferation, a major obstacle for tumor suppressor gene therapy (page 869, col. 1). With respect to modulating apoptosis in tumor cells, the reference discloses that "current vectors are far from achieving *in vivo* the requisite high levels of tumour cell modification," and that the complexity and redundancy of signaling circuits involved in apoptosis may require modulation of several components to provoke apoptosis *in vivo* (page 871, col. 2). The reference points out that because mutation compensation strategies modulate intracellular responses, that nearly all tumor cells would have to be transfected to be clinically effective, and that the current state of development of gene therapy vectors, both viral and non-viral, makes this feat unachievable within non-toxic margins of vector dose" (page 871, col. 2; page 875, col. 1).

Consequently, quantitative transduction into tumor cells by *in situ* administration may be essential (page 875, col. 1). Table 5 of Gomez-Navarro briefly summarizes advantages and disadvantages of various vector systems, notably non-viral delivery suffered from inefficient delivery and transient expression, retroviral vectors are unstable *in vivo,* and adenoviral vectors induce potent immune response. At best, the results in Xia suggest what might happen were it possible to transfect all tumor cells. However, as indicated in Orkin and Gomez-Navarro such degree of transfection was not achievable with prior art methods.

With respect to claim 14, Applicant's arguments have been addressed above regarding the lack of guidance on the recited cytoskeletal anchoring peptides. With respect to claim 15, Applicant asserts that one of skill in the art would be able to make variants of SSeCKs having higher affinity for cyclin D using the assay provided in the specification to identify them, and that this activity would not constitute undue experimentation. It has long been recognized in the chemical arts that the unpredictability of a particular art area may alone provide a reasonable doubt as to the accuracy of a broad statement made in support of the enablement of a claim. *Ex parte Singh*, 17 USPQ2d 1714, 1715 (BPAI 1991), *In re Marzocchi*, 169 USPQ 367, 369-370 (CCPA 1971). As set forth in *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

It is clear that one could not predict those changes required to increase the affinity of SSeCKs for cyclin D, and the specification fails to teach what changes to make, i.e. it fails to provide even a single example of the required SSeCKs variant. The trial and error experimentation suggested by Applicant as a remedy to this lack of guidance would constitute undue experimentation, regardless of how simple the procedure, because of the lack of guidance, lack of working examples, and the unpredictability of the endeavor.

A patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. Tossing out the germ of an idea does not constitute an enabling disclosure. While every aspect of a generic claim need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable the skilled artisan to understand and carry out the invention. It is true that a specification need not disclose what is well known in the art. However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. The rule that a specification need not disclose that which is well known in the art simply means that omission of minor details does not cause a specification to fail the enablement requirement, and is not a substitute for an enabling disclosure. However, if there is no disclosure of starting materials and of conditions under which the process can be carried out, undue experimentation is required. Failure to provide such teachings can not be rectified by asserting that the disclosure of the missing necessary information was well known in the prior art. See *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 101, 1005 (CA FC, 1997). The specification does not disclose any cytoskeletal anchoring peptides nor does it disclose any variants of SSeCKs with higher affinity for cyclin D.

Claim Rejections - 35 USC § 102

Claim 13 remains rejected under 35 U.S.C. 102(a) and (b) as being clearly anticipated by Lin et al. (Mol. Cell. Biol. 15 (5): 2754-2762, May 1995) or Lin et al.(Cancer Res. 57(11): 2304-2312, 01 June 1997) for the reasons of record set forth in the Office action of 12/18/02.

Applicant's arguments filed 6/14/04 have been fully considered but they are not persuasive. Claim 13 has been amended to recite the SSeCKs polypeptide includes a CY domain and argues that Lin does not teach that SSeCKs binds to cyclin D or the region of SSeCKs that binds to cyclin D. However, the CY domain of SSeCKs and its binding to cyclin D are inherent properties of the SSeCKs polypeptide. The material used by Lin is the same as disclosed, and the steps required by the method are disclosed in Lin. Whether Lin was aware of the molecular basis for the observed inhibition of proliferation is irrelevant to anticipation. MPEP 2112.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy J. Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott D. Priebe
Primary Examiner
Art Unit 1632